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## USSR WORK ON THE APPLICATION OF ANTIBIOTICS IN THE FOOD INDUSTRY

Vestnik Akademii Nauk SSSR Vol 24, No 5, pp 44-48 Moscow, May 1954

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[Numbers in parentheses refer to appended bibliography.]

The idea of using the antagonistic effects between microbes for combating pathogenic microorganisms had been originally suggested by I.-I. Mechnikov. However, practical application of the phenomenon of artagonism between microbes was first attempted in the 1940's, when antibiotics (tyrothricin, penicillin, and gramicidin) were isolated in a pure state.

Modern medicine and veterinary medicine have found in antibiotics a powerful means of combating infectious diseases. It is understandable that the question was raised in regard to the use of antibiotics for the control of harmful microorganisms in some industrial fields as well, particularly in the food industry for the preservation of food products from spoilage (1).

Many investigators, particularly abroad, attempted to apply for this purpose antibiotics which are known and have received extensive application in medicine, namely penicillin, streptomycin, chloromycetin, aureomycin, terramycin, subtilin, gramicidin, etc. The investigations that have been carried out dealt mainly with the problem as to whether the antibiotics mentioned are suitable for the preservation of meat, fish, and milk from spoilage. Notwithstanding certain contradictions which are encountered in published articles, it may be considered as an established fact that small quantities of antibiotics, after being added to the food product or to the ice in which the food product is kept, prevent spoilage for a certain time.

However, none of the antibiotics used in medicine have found practical application in the food industry. The principal reason for this is the natural apprehension that as a result of prolonged consumption of antibiotics microbial forms which are resistant to antibiotics will arise. Experience shows that persons who had been treated with antibiotics develop resistant forms of bacteria in their bodies with relative ease. It is obvious that after the development in the organism of microbes which are resistant to a definite antibiotic, treatment with this antibiotic of the disease produced by the microorganism in question will not succeed. In other words, the application of an antibiotic in the food industry may lead to the result that an effective therapeutic agent will be lost.

On the other hand, there still is no information worth mentioning on the nature of the effect which small doses of antibiotics administered for a long time exert on the human organism.

The rather extensive date pertaining to the action of antibiotics on animals are very contradictory. It was established that addition to the feed of minute quantities of penicillin, streptomycin, chloromycetin, aureomycin, or other antibiotics in some cases, but not always, has a trafficial effect on animals, particularly young animals. It was established that the identical antibiotics exert a different reaction on different animals. The best results were achieved with aureomycin, terramycin, and bacitracin. The mechanism of this prolonged action of antibiotics has not been investigated adequately as yet. But a number of authors assume, not without reason, that improvement in the growth of young animals, which has been noticed after the



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administration of an antibiotic in the feed, is produced principally by profound changes in the composition of the intestinal microflora and that these changes are brought about by the action of the antibiotic. It has been established that some antibiotics suppress the development of the microflora, which is harmful to the organism, for instance the putrefactive and toxicogenic microflora; while the useful microflora (lactic acid bacteria and some others), among which there are species which synthesize vitamins needed by animals, is

However, there are indications that the prolonged administration of antibiotics for therapeutic purposes may lead to a vitamin insufficiency as a result of the modification of the intestinal microflora. Other undesirable results may also arise. It has also been established that the systematic administration of antibiotics to ruminants, in the nutrition of which microbiological processes are of great importance, processes taking place in the stomach (or rather the compartment of the stomach which is called the rumen) eliminate the useful microflora and bring about severe disturbances of the digestion. In young ruminants, particularly calves during the earlier period of their life, when the microflora of the rumen does not yet play a very active role in their digestion, these disturbances are not observed.

Thus, the data of some authors, who point out the useful effect of the addition of antibiotics to the feed of animals, differ from the date published by other authors, who have not observed any such effect or who indicate that there is a harmful effect on the organism. It is not surprising that in a number of countries the sale of antibiotics to be used as an ingredient of the feed of animals is prohibited.

What has been said leads to the conclusion that our knowledge of the action of antibiotics when administered together with food is still inadequate. For that reason one must be very careful in approaching the problem on the utilization of antibiotics in the food industry. The most thorough and many-sided investigations on this subject are essential.

Very original and, from the standpoint of this discussion, very promising investigations are under way on the application in the food industry of the antibiotic properties of higher plants. Work on this subject has been done in the Soviet Union.

The juice of many higher plants, as has been shown by Soviet scientists, particularly B. P. Tokin, contains the so-called phytoncides, which have antibacterial properties (2). The phytoncides, just like antibiotics, comprise substances of the most diverse chemical composition. At present the chemical composition of many phytoncides has been investigated and these phytoncides have been isolated in the pure state.

It is obvious that in order to find out whether phytoncide preparations can be used as preservatives for food products one must investigate the effect of prolonged administration of these substances together with food. However, with reference to some food products, this problem is not of particular some canned preserves, one may effectively use the phytoncidic properties of the raw material from which these preserves are made.

Of particular interest in this respect are the investigations which have been conducted at the All-Union Scientific Research Institute of the Food Preserve Industry. These investigations established that phytoncides are contained in many vegetables and fruit as well as in some plants which are used



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as spices (3). Thus, phytoncites are contained in tomatoes, carrots, beets, horseradish, parsley, onions, pepper, mustard, and coriander. The phytoncidic properties of plants depend on their species and age. The antibacterial activity of some phytoncides is more pronounced after heating.

Under the effect of the phytoncides of vegetables, the quantity of microorganisms in canned preserves is reduced prior to sterilization. This makes it possible to reduce the temperature and extent of the sterilization of vegetable preserves by heating. The preserves obtained by the new method, which indexes of bacterial sterility.

In many plants, for instance the onion, the volatile fraction of the phytoncides is of particular value. However, this fraction may be used up in a in establishing the technological conditions for the treatment of the raw material in question.

The investigations described are of great significance from the standpoint of the fundamental principles involved. They made possible an entirely new approach, namely utilization of the antibacterial properties of the raw material being preserved, and at the same time demonstrated that on the basis of this principle one may achieve an improvement in the quality of production, prime cost.

It is obvious that further work along this line is of importance. The attention of investigators must be concentrated on the selection and introduction into the food preserving industry of those species and varieties of vegetables, fruit, and other plants which are rich in phytoncides. Furthermore, the technological processes for the treatment of such raw material must be contained in it. It is also necessary to conduct work on the phytoncidea using phytoncides in other branches of the food industry. From this standpoint, the capacity of some phytoncides to suppress the development of the putrefaction microflora which brings about spoilage of fresh fish is of great interest (4):

Soviet scientists are developing a new and original line of research dealing with the utilization of the phenomenon of interbacterial antagonism for the improvement of the quality of food products and of their stability

Organisms which exert an antibiotic effect are found within all groups of microbes, including yeast, lactic acid bacteria, acetic acid bacteria, and other species of microorganisms on the life processes of which many branches of the food industry depend. However, the products obtained with the aid of such microorganisms are often subjected to spoilage produced by extraneous microflora. Thus, sweet butter in storage loses many of its valuable properties as a result of the activity of putrefactive microorganisms, lipolytic bacteria, mold fungi, and other microorganisms.

Soviet scientists have established that some strains of yeast have the capacity of suppressing microorganisms which damage butter (5). These strains of yeast may be used for the purpose of increasing the stability of butter to spoilage. A number of strains of lactic acid streptococci, which exert an antibiotic effect on the causative factors of the spoilage of butter, have been isolated from natural sources (6). If these strains are included in the production stock culture, which is used in the manufacture of sweet butter and



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which consists of a mixture of strains of lactic acid streptococci, one may suppress the development of putrefactive organisms and other harmful microorganisms in the butter.

These investigations deserve serious attention. It is not impossible that one may discover among lactic acid bacteria cultures which have not only antibacterial activity but also antifungus activity, and the property of suppressing bacterial phages. The discovery of lactic acid bacteria that have the last-mentioned property would be of great significance for the cheese industry, where the problem of the control of bacteriophage is of great importance. The phenomenon of antagonism between microorganisms may also be successfully used in other branches of the food industry.

In January 1954 the Institute of Microbiology, Academy of Sciences USSR, conducted a conference at which a report by N. A. Krasil'nikov was presented. This report dealt with the scientific basis of the application of antibiotics in the food industry and the prospects of such application. A number of other reports on research in this field was also presented.

The conference noted the importance of continuing work on the utilization of antibiotics and phytoncides, and the application of the phenomena of antagonism between microbes in various branches of the food industry. In the action of antibiotics on the human organisms, when these antibiotics are used as preservatives for food products, the conference recommended that the appropriate institutes of the Ministry of Public Health USSR, particularly the Institute of Nutrition of the Academy of Medical Sciences USSR, take steps to

It was especially indicated that there is a necessity for expanding work aimed at the discovery of new antibiotics derived from actinomycetes, mold fungi, and bacteria, as well as of phytonoides and antibiotics of animal origin, suitable for use in the food industry.

Introduction into the food industry of new antibiotics which are not used in medicine presents, as has been stated, definite advantages. It is obvious that the selection of a new antibiotic preparation for use in the food industry must be based on all the properties of this preparation. In medicine and veterinary medicine, an antibiotic usually serves the purpose of controling a definite causative factor of some disease. In the food industry, on the other hand, one must as a rule preserve the product from the harmful action of a number of microorganisms which belong to the most diverse groups. It is therefore necessary that the antibiotic have a broad range of antimicrobial activity. Furthermore, an antibiotic which is suitable for use in the food industry must have an active effect on definite species of microorganisms not only in vitro, but also in the food product. It must be devoid of toxic properties, and harmless to the organism on prolonged consumption in small doses. It must not confer an unpleasant taste or odor, and must not produce any other undesirable changes in the properties of the food product.

Antibiotics with properties which are useful for the food industry can be found among the most diverse microorganisms. Bacteria, fungi, and actinomycetes are among them. Actinomycetes must be regarded as the most promising group of microorganisms in that respect.

As a confirmation of this may serve the results obtained in a search for antagonists effective against a number of species of microbes which produce spoilage of meat and meat products (7) Bact.coli and Bact. proteus were used as test cultures; also Penicillium, Cladosporium, and Mucor fungi. A total of 806 strains of actinomycetes were tested. Of this total 244 strains, or





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30%, exhibited the capacity for suppressing the development of either one or several of the harmful cultures used in the tests, while several had an effect on all the harmful cultures used. Antibacterial properties were exhibited by only 27 cultures, and antifungus properties by only 134 cultures, while 83 cultures suppressed the development of both bacteria and fungi present in

One must assume that cultures which have antifungus properties will prove to be a promising source of antibiotics for use in those branches of the food industry where mold fungi have to be combated.

Antibiotics which have a low thermal stability and a relatively high degree of inactivation during storage with a food product may prove to be very useful. Such antibiotics would be very suitable for application in the canning industry and other branches of the food industry. Antibiotics of this type would lower the bacterial count of the crude material or intermediate products, and at the same time make possible the application of a milder sterilization process. The subsequent inactivation of the antibiotics as a result of thermal treatment or storage would remove all possibilities of an undesirable effect of the antibiotics on the human organism.

It is understandable that introduction of antibiotics for use as food preservatives will necessitate precise methods for their quantitative deter-

The problem of the application of antibiotics in the food industry is  ${\bf a}$ new one which has not been investigated to any great extent as yet, and requires extensive study. For the successful solution to this problem the joint efforts of microbiologists, biochemists, technologists, hygienists, and representatives of other fields of knowledge are essential. In conclusion, one must point out that the expansion of work on new antibiotics will not only be of use to the food industry, but may result in discoveries which will be very valuable to medicine and agriculture.

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